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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,508	09/22/2000	Henry E. Young	1304-1-019CIP	1973

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EXAMINER	
TON, THAIAN N	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,508	YOUNG ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment and Response, filed 7/13/06, has been entered. Claims 14-17 are amended, pending and under current examination.

The Young Declaration, filed 7/13/06, has been fully considered and the Examiner responds to the Declaration and Applicants' arguments below.

Double Patenting

The prior rejection of claims 14-17 as being provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application No. 11/029,763 is withdrawn in view of the examination of a separate invention in the '763 application.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application No. 10/443,663. This rejection is maintained for reasons of record advanced in the Office action, mailed 1/12/06.

Applicants' Arguments. Applicants argue that because the '663 application is a copending application, and has recently initiated formal prosecutions, Applicants will readdress this issue at such time as when other patentability issues are settled (p.4 of the Response).

Response to Arguments. These arguments have been fully considered, but are not persuasive because Applicants have not filed an appropriate terminal disclaimer, nor provided arguments as to show why the co-pending claims are not patentably distinct, the prior rejection of record is maintained.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to genetically engineered pluripotent embryonic-like stem cells, and methods of producing the same. The '663 claims are directed to genetically engineered pluripotent embryonic-like stem cells. The instant claims are directed to isolated pluripotent embryonic-like stem cells, which are derived from non-embryonic or postnatal animal cells or tissues, capable of self-renewal and capable to differentiation to cells of all endodermal, ectodermal, and mesodermal linages, and do not give rise to functional gametes. The instant claims differ from the '663 claims in that they recite that the cells do not give rise to functional gametes. However, the instant claims are rendered obvious by the '663 claims, because they are both directed to the same types of cells, and methods of producing the same, and that the instantly claimed cells encompass cells with the same function (*i.e.*, not giving rise to functional gametes) as claimed in the '663 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". This rejection is maintained for reasons of record, advanced in the prior Office actions, mailed 1/12/06 and 4/19/05.

Applicants' Arguments. Applicants' argue that the amendment to the claims (filed 1/21/05) which state that the cells, "do not give rise to functional gametes" has support in the instantly-filed specification with regard to the pluripotent embryonic-like stem cells, which by definition and character are not totipotent cells and thereby do not give rise to functional gametes. Applicants argue that the specification, combined with the knowledge in the art enables the skilled artisan to make and/or use the invention and the claimed genetically engineered stem cells. Particularly, Applicants argue that a pluripotent is 1) not a totipotent cell (which gives rise to every type of body cell, including somatic cells and gametes) and 2) pluripotent cells only have certain differentiative capacities of a totipotent cell, particularly, in that a pluripotent cell is more limited in capacity than a totipotent cell. Applicants argue that the specification teaches that ES cells are totipotent,

and thus, give rise to all somatic lineages, as well as functional gametes. Applicants point to page 3, lines 29-31, for teachings to show that ES cells are totipotent, and argue that because the claimed cells are pluripotent, they do not form functional gametes. See p. 5 of the Response. Applicants provide alternative definitions of the term "totipotent" to argue that ES cells are totipotent (i.e., give rise to functional gametes). Applicants argue that in contrast, the instantly-claimed cells are derived from non-embryonic or postnatal tissue, and their PPELSCs are pluripotent, that a pluripotent cell is not presumed to have totipotent capacity. Applicants argue that those of skill in the art would know that a pluripotent cell lacks the ability to form gametes, and in fact, a pluripotent cell is recognized as being derived or differentiated from a totipotent stem cell. See page 6 of the Response.

Response to Arguments. These arguments are fully considered, but are not persuasive. Although the specification teaches that ES cells are totipotent and can give rise to functional gametes, this is not an indication that pluripotent cells cannot give rise to functional gametes. That is, Applicants' statement that totipotent cells can give rise to functional gametes does not preclude pluripotent cells from also producing functional gametes. In fact, pluripotent cells can, and do, give rise to functional gametes if integrated into the germline of a chimeric animal, for example (see Piedrahita, cited in the prior Office actions). It is reiterated that the specification is silent with regard to the formation of gametes using the instantly claimed cells. In fact, Applicants use the definition of "totipotent" to describe ES cells, however, the Examiner provides Roach and McNeish (*Methods for the Isolation and Maintenance of Murine Embryonic Stem cells*, from Embryonic Stem Cells, Methods and Protocols, Ed. Turken, Humana Press, 2002, pages 1-2) who clearly describe ES cells as "pluripotent", and that "Smithies and colleagues later demonstrated that ES cells, modified by gene targeting when reintroduced into blastocyst, could transmit the genetic modification through the germline." See

p. 1, lines 6-8, *emphasis added.* This is further supported by Yu and Thomson (*Embryonic Stem Cells*, from Regenerative Medicine 2006, Department of Health and Human Services. August 2006. /info/scireport/2006report, pages 1-12) who show that totipotent cells are, in humans, found at day 3 after fertilization, whereas plruipotnet ES cells, which are isolated from the ICM of the blastocyst are found at day 5 after fertilization (see page 1, figure 1.1). Clearly, ES cells, which are isolated from blastocysts, are not art-recognized as "totipotent". Further, Figure 1.2 (page 2) shows defines plruipotency as, "ES cells can give rise to cells from all three embryonic germ layers even after being grown in culture for a long time." They show examples of cell types that are derived from each layer, and that germ cells (sperm or eggs) are derived from the endoderm. Thus, it is clear that the art-recognizes that the term *pluripotent* encompasses cells that can (but are not required) to differentiate into cells that form functional gametes.

Thus, as stated in prior Office actions, it is not an art-recognized property that a pluripotent stem cell cannot give rise to functional gametes. There are circumstances, as shown previously, where they can do so, or alternatively, where they do not form functional gametes. There is no question that totipotent cells are less differentiated than pluripotent cells, the issue at hand is whether or not pluripotent cells can produce functional gametes. The art clearly shows that pluripotent cells have this capability. Therefore, the definition suggested by Applicants is not art-recognized, and it is also reiterated that the specification provides no literal support for the recitation of pluripotent stem cells that cannot give rise to functional gametes. Thus, the as-filed specification fails to provide specific, literal support for this recitation and it is properly determined to be new matter.

Applicants' Arguments and the Young Declaration.. Applicants provide the Young Declaration which shows that the instantly-claimed PPELSCs have not been demonstrated to form gametes. The Declaration teaches attempts by the inventor to

identify the formation of gametes from the pluripotent embryonic-line stem cells, and at the filing of this application, and subsequent to the date of filing, have been unsuccessful. Applicants argue that because it was found that BLSCs, another population of stem cells, could give rise to gametes under the same conditions of PPELSCs, that it is clear that the PPELSCs of the instant invention do not give rise to functional gametes.

The Young Declaration cites the paper "Adult-Derived Stem cells" which describes various categories of stem cells located within adult or postnatal tissues, and particularly, the instantly claimed PPELSCs (pluripotent embryonic-like stem cells) can form somatic cells from 3 primary germ layer lineages, but will not form sperm or ova. The Declaration points to the Abstract and Table 1. This is contrasted to blastomere-like stem cells (BLSCs) which can form all somatic cells and spermatogonia, as noted in Table 1. The Declaration states that the PPELSCs of the instant invention are the same as those designated ELSCs in the paper, and thus, the instantly claimed cells cannot form gametes. See pages 2-3, #6-7 of the Declaration).

Response to Arguments. These arguments have been considered, but are not persuasive. Firstly, it appears that the determination of the stem cells to produce various cell lineages is based on *in vitro* assays, using lineage induction agents, various hormones or growth factors. That is to say, that the instantly-claimed cells do not appear to produce functional gametes *in vitro*. There is no guidance as to if the PPELSCs are capable of forming functional gametes *in vivo*. The art that has been previously provided shows that pluripotent cells, isolated from a variety of sources, are capable of contributing to the germ line when used to produce a chimeric or transgenic animal. The instantly-provided specification and arguments show that there are no functional gametes that are produced *in vitro*, but does not provide guidance for a scenario where the cell is introduced *in vivo*. Thus, this does not provide guidance for the full breadth of the phrase "do not give rise to functional

gametes". It is further reiterated that specification provides no literal support for the instantly-claimed cells with regard to their inability to give rise to functional gametes, and thus, this amendment is deemed to be new matter.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 14-17 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Capecchi *et al.* [**Scientific American**, 270(3):34-41 (1994)]. This rejection is maintained for reasons of record, advanced in the prior Office actions, mailed 1/12/06, 4/19/05, and 10/19/04.

Applicants' Arguments. Applicants argue that Capecchi does not anticipate the claimed invention because the ES cells of Capecchi are "totipotent" and can and do give rise to gametes, by definition, whereas the pluripotent embryonic-like stem cells of Applicants cannot. (*Emphasis in original*). Applicants argue that the claim only requires a single cell that does not give rise to functional gametes, and thus, Applicants have amended the claims to a plurality of cells. Furthermore, Applicants argue that the claimed ELSCs, when grown under inducing conditions, as a population of isolated cells do not form gametes, as evidenced by the Young

Declaration. Applicants argue that ES cells are totipotent, not pluripotent, and that Applicants' pluripotent cells cannot form gametes, and thus, are not anticipated by the claimed invention. See page 7 of the Response.

Response to arguments. These arguments are fully considered, but not persuasive. As stated above, and in prior Office actions, although Capecchi's cells are isolated from a different source, they fulfill the limitations of the claims because they are transfected, isolated, pluripotent cells which can differentiate into cells derived from all three germ layers, and do not give rise to functional gametes. The NIH stem cell information (cited previously) and the Roach citation (above) which provides a definition for pluripotent cells, which states that, they are cells which have the capability of developing cells from all germ layers. The ES cells taught by Capecchi do not fulfill the definition of "totipotent" stem cells, because they cannot produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. There is no specific definition provided by the instantly-filed specification to show that pluripotent cells can never produce functional gametes. The Declaration, to which Applicants point to as evidence to show that their cells do not form functional gametes, is not persuasive, because the evidence relates only to *in vitro* experiments, and does not show that the ELSCs never produce functional gametes. Finally, even amending the claims to a plurality of cells fails to overcome this rejection, because when producing transgenic/knockout mice, one of skill in the art would know that initially, one produces chimeric mice, which need to be screened for the germline transmission of the transgene (*i.e.*, the transmission via the ES cells). Thus, clearly, ES cells sometimes do, and at other times, do not, contribute to the germline. Clearly chimeric mice produced from ES cells that do not have germline transmission are examples of cells that do not give rise to functional gametes. Accordingly, this rejection is maintained.

The claims state that the cells are "derived from non-embryonic or postnatal animal cells or tissues." However, this requirement is a product made by a particular process. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Thus, because Capecchi teach cells that are pluripotent, by Applicants' definition, they anticipate the claims.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Piedrahita *et al.* This rejection is maintained for reasons of record, advanced in the prior Office action mailed 1/12/06 and 4/19/05.

Applicants' Arguments. Applicants argue that Piedrahita *et al.* do not anticipate the claimed invention, because their cells are absolutely distinct from the pluripotent embryonic-like stem cells of the instant invention. Namely, Applicants argue that the chimeric cells of Piedrahita *et al.* contributed to the germ line, and that their cells are thus "totipotent", and that Applicants' cells cannot produce

gametes, they are "pluripotent". Applicants argue that their PPELSCs do not possess all the capabilities of Piedrahita's cells, and thus, are distinct from them. See pages 7-8 of the Response.

Response to Arguments. These arguments are fully considered, but not persuasive. As stated previously, totipotent cells are those which produce *extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs.* Although Applicants' definition states that totipotent cells can form functional gametes, there is no definition provided by Applicants to show that pluripotent cells can never form functional gametes. Piedrahita further define their cells as pluripotent, which is within the art-recognized definition of the term (see also, the definitions provided above). It is reiterated that upon formation of a chimeric animal, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. Furthermore, as stated above and previously, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the PGCs taught by Piedrahita *et al.* Finally, even amending the claims to a plurality of cells fails to overcome this rejection, because when producing transgenic animals, one of skill in the art would know that initially, one produces chimeric animals, which need to be screened for the germline transmission of the transgene (*i.e.*, the transmission via the pluripotent cells). Thus, clearly, pluripotent cells (in this case, PGCs) sometimes do, and at other times, do not contribute to the germline. There is nothing in the claims that state that the claimed cells can never form functional gametes. Thus, evidence that cells that do not contribute to the germline fufill the limitations of the claims.

Piedrahita *et al.* anticipate the claimed invention because the PGCs they teach are capable of differentiation into the three germ layers (as evidenced by both the generation of embryoid bodies and the generation of chimeric pig fetuses and chimeric piglets). Chimeric animals, by definition, have some cells have cells that

are contributed by the donor cells, and some from the cells of the recipient blastocysts. Piedrahita teach the analysis of transgene expression and show that the pigs expressed the transgene in different tissues, they teach that analysis of the developing fetuses which suggests that although some may have germ line transmission, it would require that the chimeric cells contribute to the germ line. See p. 1328, 2nd column, 2nd full ¶, and p. 1329, 1st column, 2nd ¶. Thus, this analysis provides evidence that the pluripotent cells could not contribute to the germline in certain chimeric animals.

Accordingly, Piedrahita anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamblott when taken with Sambrook *et al.* This rejection is maintained for

reasons of record, advanced in the Office actions mailed 1/12/06, 4/19/05 and 10/19/04.

Applicants' Arguments. Applicants argue that they have now changed their to a plurality of cells, and that the claimed ELSCs, when grown under inducing condition as a population of isolated do not form gametes, as evidenced by the Declaration. Applicants further argue that now the claims are amended to recite a plurality of cells, and thus, the claims are not rendered obvious over the recited art.

Response to Arguments. These arguments are fully considered, but are not persuasive. As stated previously, the cells of Shamblott are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Although pluripotent cells have the ability to colonize the germline (as stated by Shamblott, and cited by Applicants), the cells also have the ability to differentiate to other cells, as evidenced by the production of chimeric animals. For example, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. The claims do not recite that the instantly-claimed cells can never form functional gametes, merely that they do not. Thus, given that pluripotent cells have art-recognized characteristics to differentiate into various cell types, this encompasses circumstances where cells would not contribute to the germline.

Furthermore, as stated above and previously, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the PGCs taught by Shamblott. Shamblott teaches that the PGCs are pluripotent, as are the claimed cells. The specification teaches that a pluripotent stem cell is capable of self-regeneration, differentiation to cells of endodermal, ectodermal and mesodermal lineages (see p. 35-36). Thus, the cells of Shamblott fulfill the limitations of Applicants' definition of "pluripotent".

Shamblott *et al.* teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells [PGCs] and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers [see *Abstract*]. In particular, Shamblott *et al.* teach that gonadal ridges and mesenteries of 5 to 9 week old human fetuses and cells initially cultured on a layer of mouse STO fibroblast feeder layer. The cells formed embryoid bodies, which were collected and analyzed immunohistochemically [see pp. 13726-13727, *Materials & Methods*]. It was found that the embryoid bodies demonstrated derivatives of the three embryonic germ layers [see p. 13729, 2nd column and Table 1]. Note that Shamblott teach the pluripotent embryonic-like stem cells because the claims do not provide any requisite characteristics (*e.g.*, specific markers, etc.) of the claimed embryonic-like stem cells such that they would be distinguished from the cells taught by Shamblott. The claims recite that the embryonic-like stem cells are "derived from non-embryonic or postnatal animal cells or tissue;" however, this recitation does not differentiate them from the cells as taught by Shamblott. Further, the method claim has been included in this rejection because the cells as instantly claimed are not distinguishable from those taught in the art. The cells as taught by Shamblott fulfill the requirements of the claims because they are capable of differentiation to cells of each and any of endodermal, ectodermal and mesodermal lineages, and are capable of self-renewal.

Shamblott do not teach the transfection of the pluripotent stem cells to produce a genetically engineered pluripotent stem cell. However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Shamblott and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the PGCs, as taught by Shamblott and transfect them with any DNA of interest, with a

reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson when taken with Sambrook *et al.* This rejection is maintained for reasons of record advanced on pages 16-17 of the Office action, mailed 4/19/05; pages 12-13 of the Office action, mailed 10/19/04.

Applicants' Arguments. Applicants argue that the Examiner is "factually incorrect" because pluripotent cells do not have the ability/capability to colonize the germline. Applicants argue that their cells cannot form gametes, and thus, assert their cells are distinct from the cells of Thomson, which are ES cells and can colonize the germ line. Furthermore PPELSCs are not made obvious by the combination of Thomson with Sambrook, because ES cells are "totipotent" and capable of giving rise to all somatic lineages as well as function gametes, and Applicants' cells are pluripotent and do not give rise to functional gametes. See pages 9-10 of the Response.

Response to Arguments. This is not found to be persuasive. As stated previously, the cells of Thomson are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Furthermore, although pluripotent cells have the ability/capability to colonize the germline, pluripotent cells also have the ability to differentiate to other cells, as evidenced by the

production of chimeric animals. Furthermore, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the pluripotent cells, as taught by Thomson. Thomson teaches that the isolated cells are pluripotent, as are the claimed cells. The specification teaches that a pluripotent stem cell is capable of self-regeneration, differentiation to cells of endodermal, ectodermal and mesodermal lineages (see p. 35-36). Thus, the cells of Thomson fulfill Applicants' definition of the term "pluripotent".

Thomson teach the isolation of ES cells from the rhesus monkey. See p. 7844, *Materials and Methods*, col. 2. The cells are capable of maintaining an undifferentiated state and proliferate indefinitely, and have the potential to differentiate into derivatives of all three embryonic germ layers. They teach that the cells differentiated into cells of endoderm, mesoderm and ectoderm. See *Abstract* and p. 7846, col. 1-2, bridging ¶. Note that the claims fail to distinguish the claimed cells from the cells taught by Thomson. Thus, the method claim has been included in the rejection because the cells used in the method are not distinguished from those taught by Thomson. Thomson do not teach that the ES cells are genetically engineered to express a gene or protein of interest.

However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Thomson and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the pluripotent embryonic stem cells, as taught by Thomson and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the

biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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